International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN: 2347-6567

IJAMSCR |Volume 3 | Issue 4 | Oct-Dec- 2015
www.ijamscr.com

Research article *Medical research*

Vitamin D status and its association with blood glucose parameters among Indian diabetic patients: A non-interventional, cross-sectional, Observational study

Praveen Raj, Rahul Balip*, Kamlesh Patel, Vishal Vaidya

Abbott Healthcare Pvt Ltd, Mulund (West), Mumbai 400080, India

***Corresponding Author: Dr. Rahul Balip**

ABSTRACT

INTRODUCTION

The aim of the study was to evaluate vitamin D status and its association with blood glucose parameters in Indian diabetic patients.

MATERIALS AND METHODS

This cross-sectional, non-interventional, single visit program was conducted across 236 sites in India where 4434 (males: 2580; females: 1854) diabetic patients of 18-65 years of age who had undergone testing for vitamin D and blood glucose in the last 3 months were recruited in the study. Anthropometric and metabolic parameters, and serum 25-hydroxyvitamin D (25[OH] D) was measured. The patient was said to have 'non-optimal level of vitamin D' if had serum 25(OH) D <30 ng/mL ('vitamin D deficient' <20 ng/mL, 'vitamin D insufficient' 20-29 ng/mL) and was said to have 'optimal level of vitamin D' if the level was ≥30 ng/mL. Descriptive statistics was used in the study.

RESULTS

99.0% patients had type 2 diabetes and 1.0% patients had type 1 diabetes mellitus. 81.7% of the patients had 'not optimal' level of 25(OH)D where 41.5% patients had 25(OH)D deficiency and 40.2% patients had 25(OH)D insufficiency and 18.3% of the patients had 'optimal' level of 25(OH)D. Mean level of 25(OH)D was 22.1 ± 7.9 ng/mL. Higher proportion of patients with 'not optimal' level of 25(OH)D had a higher range of fasting plasma glucose (FPG; 135-298 mg/dL), glycated hemoglobin (HbA1c; 8.3-13.8%), and postprandial glucose (PPG; 217-299 mg/dL) as compared to patients with 'optimal' level. In addition, a negative correlation was found between 25(OH)D levels and calcium and a positive correlation with height and body mass index.

CONCLUSION

Despite an ample amount of sunlight in the country, 81.7% of Indian diabetic patients had deficient or insufficient levels of vitamin D (25[OH]D <30 ng/mL). The level of vitamin D had a negative correlation with FPG, PPG, HbA1c and serum calcium; suggesting that vitamin D supplementation may improve glycaemic control in diabetic patients.

KEY WORDS: Vitamin D, diabetes, insulin resistance, glycated hemoglobin

INTRODUCTION

Diabetes mellitus (DM) is the most common metabolic disorder characterized by hyperglycaemia and insulin resistance [1]. According to International Diabetes Federation, the prevalence of diabetes in India is likely to increase from 61.3 million (in 2011) to 101.2 million (in 2030) with a global estimate of 552 million by the year 2030 [2]. Several factors, including nutritional conditions, genetics, lifestyle, and environmental conditions play an important role in increasing the risk of DM [3]. Vitamin D, a nutritional factor, not only regulates serum calcium and bone health but also plays an important role in glycaemic control by improving β-cell function and insulin sensitivity related to expression of insulin receptor, and by inhibiting β-cell apoptosis [4-6]. The economical and a major source of vitamin D is sunlight exposure for about 10 to 15 minutes thrice a week where 7-dehydrocholesterol in skin is converted to previtamin D3 which is further metabolized in the liver to 25-hydroxyvitamin D (25[OH]D), the major circulating metabolite and a marker of vitamin D status. In the kidney, 25(OH)D is metabolized to its active form 1,25-dihydroxyvitamin D (25[OH]2D) by 1-alpha-hydroxylase enzyme [7]. The other natural sources of vitamin D are fish, oils, mushrooms, beef liver, cheese, egg yolk; but all of these natural sources provide trace amount of vitamin D which is inadequate for normal body requirements [8]. Hence, vitamin D fortified foods have been commercialized to meet the level of vitamin D in our daily diet. Though there is ample of sunlight in Asian countries but vitamin D deficiency still prevails in Indian population; the reason may be restricted human exposure to sunlight, dark skin pigmentation, obesity, vegetarian dietary habits, low intake of vitamin D fortified food, and lifestyle factors like indoor working or working in a close environment with minimum sun exposure. More than 70% of the Indians are reported to have vitamin D deficiency [9-13]. In 2012, Pittas et al. showed an inverse relationship between plasma 25(OH)D and risk of diabetes in high risk patients [14]. Various Indian studies have reported vitamin D deficiency in Indian diabetic patients and significant lower levels of 25(OH)D in type 2 diabetes mellitus (T2DM) patients as compared to the control group [15-17]. In 2010, Borkar et al. reported significantly lower levels of 25(OH)D in diabetic children aged 6-12 years as compared to healthy children (20.02 ± 10.63 ng/mL versus 26.16 ± 12.28 ng/mL; P = 0.009) [15]. In another study published in 2011, 57.6% of T2DM patients had severe vitamin D deficiency as compared to 33.3% of non-diabetic patients (P = 0.001) [16]. In a prospective case control study in north India, 91.1% of diabetic patients opposed to 58.5% of healthy controls were reported to have vitamin D deficiency. In addition, diabetic patients had significantly lower levels of 25(OH)D than the control group (7.88 ± 1.20 ng/mL versus 16.64 ± 7.83 ng/mL) [17]. There is limited published literature on association of 25(OH)D levels and glycaemic parameters in diabetic patients, hence the present observational program was planned over a large scale to evaluate the correlation between 25(OH)D levels and glycaemic parameters in Indian diabetic patients.

MATERIALS AND METHODS

The present cross-sectional, non-interventional, and a single visit program was conducted across 236 sites (Uttar Pradesh, Gujrat, Punjab, Maharashtra, Karnataka, Madhya Pradesh, Kerala, Delhi, Haryana, Rajasthan, Jammu and Kashmir, West Bengal, Jharkhand, Andhra Pradesh, Tamil Nadu, Bihar, Uttarakhand, Assam, Himachal Pradesh and Chhatisgarh) in India over a period of 1 year (January-December 2014). In this program, 4434 diabetic patients of 18-65 years of age who visited their physician for a routine check-up at the outpatient department, had undergone testing for vitamin D and blood glucose in the last 3 months, and were able to communicate meaningfully with the study physician were enrolled. Those patients who were already on vitamin D supplements, had a history of moderate to severe renal or hepatic disease, were debilitated, and pregnant or lactating females were excluded from the study. An institutional ethics committee approval and consent on patient authorization form was taken from all patients prior to their enrolment in the study. Vitamin D status was evaluated by measuring serum 25(OH)D. The patient was said to have vitamin D deficiency/'not optimal' vitamin D levels if he/she had serum 25(OH)D <30 ng/mL and was said to have 'optimal' vitamin D if the level was ≥30 ng/mL. Anthropometric parameters

such as weight, height and body mass index (BMI) were taken. Metabolic parameters, including fasting plasma glucose (FPG), postprandial glucose (PPG) levels, glycated hemoglobin (HbA1c), biochemical parameters (alkaline phosphatase, calcium and phosphorous), blood pressure were measured in this program. In addition, their smoking and alcohol habits, average duration of daily sun exposure, medical history, treatment history of last 3 months, comorbid conditions were also recorded in Abbott defined web based case report form. The study endpoints were to evaluate the 1) proportion of vitamin D deficient patients, 2) association between vitamin D deficiency and glycaemic parameters and 3) correlation between vitamin D with anthropometric and metabolic parameters.

DATA ANALYSIS

Descriptive statistics (generated using Statistical Analysis System® version 9.3 software) was used in the study where continuous variables were presented on mean ± standard deviation (range) and the categorical variables in number (percentage). Pearson's correlation coefficient was used to find the correlation between vitamin D and anthropometric and metabolic parameters.

RESULTS

A total of 4434 diabetic patients (males: 2580 [58.2%]; females: 1854 [41.8%]) with mean age of 51.4 ± 8.4 years were enrolled in the study. Of these, 4388 (99.0%) patients had type 2 diabetes (T2DM) and 46 (1.0%) patients had type 1 diabetes mellitus. The mean duration of diabetes was 5.3 ± 4.4 years. The data for anti-diabetic therapy was available for 85.3% (3782/4434) of the patients; the most common anti-diabetic therapy was Metformin (57.5%, 2175/3782) followed by Glimepiride (27.4%, 1038/3782). More than 50% of the enrolled patients had whitish to fair complexion (65.9%, 2924/4434), indoor work profile (55.4%, 2455/4434 patients), 15 to >30 min average daily sun exposure (62.7%, 2781/4434) and 54.3% (2409/4434) patients had sun exposure during morning hours (7 AM-11 AM). Higher proportion of patients were non-smokers (76.6%, 3397/4434), non-alcoholics (78.7%, 3490/4434) and had vegetarian diet (38.1%, 1698/4434). Hypertension was the only co-morbid condition reported in >10% of the patients (25.15%, 1115/4434); the mean duration of hypertension was 5.4 ± 4.1 years. The data for concomitant medications was available for 1140 of 4434 (25.7%) patients. More than 20% of the patients were on concomitant medications that acted on renin angiotensin system (53.1%, 605/1140) (>10% of the patients were on telmisartan [62.5%, 378/605], olmesartan [17.5%,106/605] and losartan [11.9%, 72/605]) and lipid modifying agents (20.1%, 229/1140) (>10% of the patients were on atorvastatin [67.7%, 155/229] and rosuvastatin [27.5%, 63/229]). Other baseline characteristics are presented in Table 1. Overall, 25(OH) D average level was 22.1 ± 7.9 ng/mL. 81.7% (3624/4434) of the patients had 'not optimal' level of vitamin D (<30 ng/mL) where 1842 (41.5%) patients had 'deficient' level of vitamin D (<20 ng/mL) and 1782 (40.2%) patients had 'insufficient' level of vitamin D (20-29 ng/mL). The remaining 810 of 4434 (18.3%) patients had 'optimal' level of vitamin D (≥ 30 ng/mL). The higher proportion of patients in the 'not optimal' vitamin D category had FPG, HbA1c and PPG in the higher range (FPG: 135-298 mg/dL; HbA1c: 8.3-13.8% and PPG: 217-299 mg/dL) as compared to patients in the 'optimal' vitamin D category (Figure 1). Overall, vitamin D levels had a negative correlation (inverse relationship) with FPG, PPG, HbA1c and serum calcium and a positive correlation (direct relationship) with height and BMI (Pearson's correlation coefficient; Table 2). Data for Vitamin D therapy was available for only 2170 of 4434 (49%) patients; 1562 of 2170 (72.0%) patients were on cholecalciferol.

Table 1: Baseline characteristics

Category/Statistics	Total Number of Patients (N = 4434)
Anthropometric	
Age (years), mean±SD	51.4 ± 8.44 years
Height (cm), mean±SD	163.6 ± 8.53

Weight (kg), mean±SD	69.2 ± 10.25
BMI (kg/m^2), mean±SD	25.9 ± 3.66
Exposure to sunlight: indoor; outdoor, n (%)	2455 (55.4); 1330 (30.0)
Metabolic parameters	
FPG levels (mg/dL), mean±SD	135.1 ± 31.58
PPG levels (mg/dL), mean±SD	191.1 ± 43.79
HbA1c (%), mean±SD	7.67 ± 1.081
Biochemical parameters	
Alkaline phosphatase (U/L), mean±SD	135.4 ± 60.9
Calcium (mg/dL), mean±SD	8.6 ± 1.3
Phosphorus (mg/dL), mean±SD	3.7 ± 0.7
Life style of patients	
If smoking is yes: regular, occasional, missing n (%), duration of smoking (years)	356 (55.0); 243 (37.6); 48 (7.4); 11.4 ± 7.14
If alcohol intake is yes: regular, occasional, missing n (%), duration of alcohol intake (years)	117 (21.1); 407 (73.5); 30 (5.4); 11.0 ± 6.81
Vitals	
Blood pressure (mmHg), mean±SD: systolic, diastolic	135.2 ± 20.80; 84.5 ± 9.12
Comorbid conditions, n(%); duration (years), mean±SD	
Hypertension	1115 (25.2); 5.4 ± 4.1
Neuropathy	202 (4.6); 3.3 ± 2.6
Nephropathy	57 (1.3); 3.1 ± 2.2
Retinopathy	17 (0.4); 2.2 ± 1.6
Hypothyroid	188 (4.2); 6.9 ± 5.4
Hyperthyroid	37 (0.83); 4.0 ± 7.4
Cardiovascular disease	262 (5.9); 3.0 ± 2.3
Epilepsy	3 (0.1); 10.0 ± 0
Osteoporesis	51 (1.1); 2.4 ± 1.9

Table 2: Correlation between vitamin D with anthropometric, metabolic and biochemical parameters

Parameters	**Vitamin D classification**			
	Deficiency (<20ng/mL)	**Insufficiency (20-29 ng/mL)**	**Not optimal (<30 ng/mL)**	**Optimal (≥30 ng/mL)**
Anthropometric				
Height (cm)	-0.04049	0.03709	0.00811	0.05866
Weight (kg)	-0.03812	0.02237	-0.04803	0.07780
BMI (kg/m^2)	0.02299	0.03341	0.00158	0.01273
Metabolic				
FPG (mg/dL)	-0.11335	-0.08719	-0.18075	-0.10915
PPG(mg/dL)	-0.06633	-0.02001	-0.14515	-0.13314
HBA1c (%)	-0.18944	0.03985	-0.19997	-0.00620
Biochemical parameters				
Alkaline phosphatase (U/L)	-0.07709	-0.21785	-0.14291	0.31865
Calcium (mg/dL)	-0.04118	0.05200	-0.01757	-0.39283
Phosphorus (mg/dL)	0.00356	-0.13679	-0.06634	0.29247

Note: *A negative correlation is a relationship between two variables such that as the value of one variable increases, the other decreases and vice versa. A positive correlation exists when as one variable decreases, the other variable also decreases and vice versa.*

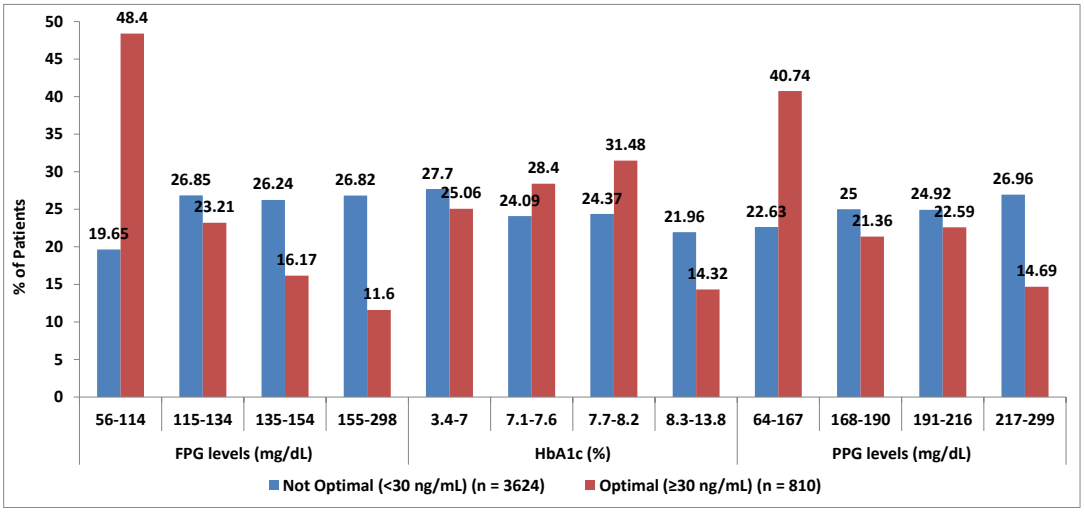

Figure 1: Association of vitamin D with blood glucose parameters

DISCUSSION

India is a vast tropical country with geographical latitude from 8.4° N to 37.6° N with majority of people experiencing ample amount of sunlight throughout the year [9-11]. But vitamin D deficiency (levels <30 ng/mL) still prevails in more than 70% of population in all age groups which may be due to their indoor work profile, sedentary lifestyle, dark skin pigmentation, vegetarian diet and obesity [9, 16-23]. Earlier studies have reported vitamin D deficiency in >80% of diabetes patients with a negative correlation with T2DM/insulin resistance [24-27], HbA1c [28-30], and fasting glucose[31]. However, few studies did not report such an inverse relationship between vitamin D levels and glycaemic status.[17,20] In addition, few studies have reported that vitamin D supplementation improve glycaemic control and insulin resistance in T2DM patients [32-35]. In our study as well, 81.7% of the diabetic patients had deficient or insufficient levels of vitamin D with a negative correlation with FBG, PPG and HbA1c levels; implying that optimal vitamin D levels may improve glycaemic control in diabetic patients. The reason for insufficient levels of vitamin D levels in Indian population may be due to indoor work profile (55.4% patients), vegetarian diet (38.1%) and higher weight (with BMI: 25.9 ± 3.66 kg/m^2). The normal hours for conversion of 7-dehydrocholesterol to previtamin D3 is reported to be between 11 AM to 2 PM. However, in our study, only 32% patients had sun exposure between 11 AM to 4 PM which further strengthened the reason for low vitamin D levels in Indian patients. The present study had few limitations 1) subjects were not on controlled diet, lifestyle and sun exposure; 2) lack of data on percentage of body fat; and 3) serum 25(OH)D was used as the only indicator of vitamin D status. No indicator to detect functional index of vitamin D was used.

CONCLUSION

The higher proportion (81.7%) of Indian diabetic patients had deficient or insufficient levels of vitamin D, despite an ample amount of sunlight. These patients have been reported to have a higher range of glycaemic parameters as compared to diabetic patients with optimal levels of vitamin D. Hence, cautious vitamin D supplementation may improve glycaemic control in diabetic patients.

ACKNOWLEDGEMENTS

The authors wish to thank all the participating investigators, site management organization & the medical writing agency for their efforts.

DISCLOSURE

This study was funded by Abbott Healthcare Pvt Ltd. Dr. Kamlesh Patel, General Manager (Medical Services), Dr. Praveen Raj, Chief Manager (Medical Services), Vishal Vaidya (Clinical Project Lead) & Dr. Rahul Balip (Medical Advisor), all working with Abbott Healthcare Pvt Ltd have authored this manuscript. All four authors have declared and confirmed that there is no financial conflict of interest with respect to the authored manuscript.

CONFLICT OF INTEREST

None declared

REFERENCES

[1]. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2011;34:S62-9.
[2]. International Diabetes Federation. One adult in ten will have diabetes by 2030. IDF Press release, 2011. Available at: http://www.idf.org/media-events/press-releases/2011/diabetes-atlas-5th-edition.
[3]. Sheth JJ, Shah A, Sheth FJ, *et al*. Does vitamin D play a significant role in type 2 diabetes? BMC Endocrine Disorders 2015;15:5.
[4]. Alvarez JA, Ashraf A. Role of vitamin D in insulin secretion and insulin sensitivity for glucose homeostasis. Int J Endocrinol 2010;2010:351-85.
[5]. Takiishi T, Gysemans C, Bouillon R, Mathieu C. Vitamin D and diabetes. Endocrinol Metab Clin N Am 2010; 39:419-46.
[6]. Mezza T, Muscogiuri G, Sorice GP, *et al*. Vitamin D deficiency: a new risk factor for type 2 diabetes? Ann Nutr Metab 2012;61:337-48.
[7]. DeLuca HF. Overview of general physiologic features and functions of vitamin D. Am J Clin Nutr 2004;80:1689S-96S.
[8]. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008;87:1080S-6S.
[9]. Harinarayan CV, Joshi SR. Vitamin D status in India-its implications and remedial measures. J Assoc Physicians India 2009;57:40-8.
[10]. Harinarayan CV, Holick MF, Prasad UV. Vitamin D status and sun exposure in India. Dermatoendocrinol 2013;5:130-41.
[11]. Ritu G, Ajay G. Vitamin D Deficiency in India: Prevalence, Causalities and Interventions. Nutrients 2014;6:729-75.
[12]. Harinarayan CV, Ramalakshmi T, Venkataprasad V. High prevalence of low dietary calcium and low vitamin D status in healthy south Indians. Asia Pac J Clin Nutr 2004;13:359-64.
[13]. Goswami R, Mishra SK, Kochupillai N. Prevalence & potential significance of vitamin D deficiency in Asian Indians. Indian J Med Res 2008;127:229-38.
[14]. Pittas AG, Nelson J, Mitri J, *et al*. Plasma 25-hydroxyvitamin D and progression to diabetes in patients at risk for diabetes: an ancillary analysis in the Diabetes Prevention Program. Diabetes Care 2012;35:565-73.
[15]. Borkar VV, Devidayal, Verma S, Bhalla AK. Low levels of vitamin D in North Indian children with newly diagnosed type 1 diabetes. Pediatr Diabetes 2010;11:345-50.
[16]. Subramanian A, Nigam P, Misra A, *et al*. Severe vitamin D deficiency in patients with Type 2 diabetes in north India. Diabetes Manag 2011;1:477-83.
[17]. Daga RA, Laway BA, Shah ZA, Mir SA, Kotwal SK, Zargar AH. High prevalence of vitamin D deficiency among newly diagnosed youth-onset diabetes mellitus in north India. Arq Bras Endocrinol Metab 2012;56:423-8.
[18]. Marwaha RK, Sripathy G. Vitamin D and bone mineral density of healthy school children in northern India. Indian J Med Res 2008;127:239-44.
[19]. Harinarayan CV. Prevalence of vitamin D insufficiency in postmenopausal South Indian women. Osteoporos Int 2005;16:397-402.

[20]. Kumar A, Haria JM. Vitamin D status and type 2 diabetes mellitus in Indians: A case-control study. International Journal of Scientific Study 2014;2:104-7.
[21]. Kumar RA, Narasimhasetty KR, Bhende PV, Lalitha R, Shetty SB. Prevalence of vitamin D deficiency in south Indian type 2 diabetes individuals. IJCCI 2014;5:15-22.
[22]. Chaudhary S, Thukral A, Tiwari S, Pratyush DD, Singh SK. Vitamin D status of patients with type 2 diabetes and sputum positive pulmonary tuberculosis. Indian J Endocrinol Metab 2013;17:S670-3.
[23]. G R, Gupta A. Vitamin D Deficiency in India: Prevalence, Causalities and Interventions. Nutrients 2014;6:729-75.
[24]. Chiu KC, Chu A, Go VL, Saad MF. Hypovitaminosis D is associated with inulin resistance and beta cell dysfunction. Am J Clin Nutr 2004;79:820-5.
[25]. Forouhi NG, Luan J, Hennings S, Wareham NJ. Incidence of Type 2 diabetes in England and its association with baseline impaired fasting glucose: the Ely study 1990-2000. Diabet Med 2007;24:200-7.
[26]. Heaney R, French C, Nguyen S, *et al*. A novel approach localizes the association of vitamin d status with insulin resistance to one region of the 25-hydroxyvitamin D continuum. Adv Nutr 2013;4:303-10.
[27]. Scragg R, Sowers M, Bell C; Third National Health and Nutrition Examination Survey. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutrition Examination Survey. Diabetes Care 2004;27:2813-8.
[28]. Pittas AG, Harris SS, Stark PC, Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. Diabetes Care 2007;30:980-6.
[29]. Kositsawat J, Freeman VL, Gerber BS, Geraci S. Association of A1C levels with vitamin D status in U.S. adults: data from the National Health and Nutrition Examination Survey. Diabetes Care 2010;33:1236-8.
[30]. Kostoglou-Athanassiou I, Athanassiou P, Gkountouvas A, Kaldrymides P. Vitamin D and glycemic control in diabetes mellitus type 2. Ther Adv Endocrinol Metab 2013;4:122-8.
[31]. Kayaniyil S, Harris SB, Retnakaran R, *et al*. Prospective association of 25(OH)D with metabolic syndrome. Clin Endocrinol (Oxf) 2014;80:502-7.
[32]. Maestro B, Molero S, Bajo S, Davila N, Calle C. Transcriptional activation of the human insulin receptorgene by 1,25-dihydroxyvitamin D(3). Cell Biochem Funct 2002;20:227-32.
[33]. Ozfirat Z, Chowdhury TA. Vitamin D deficiency and type 2 diabetes. Postgrad Med J 2010;86:18-25.
[34]. Al-Daghri NM, Alkharfy KM, Al-Othman A, *et al*. Vitamin D supplementation as an adjuvant therapy for patients with T2DM: an 18-month prospective interventional study. Cardiovasc Diabetol 2012;11:85.
[35]. Alzaim M, Wood RJ. Vitamin D and gestational diabetes mellitus. Nutr Rev 2013;71:158-67.

How to cite this article: Praveen Raj, Rahul Balip, Kamlesh Patel, Vishal Vaidya, Vitamin D status and its association with blood glucose parameters among Indian diabetic patients: A non-interventional, cross sectional, Observational study. Int. J of Allied Med Sci and Clin Res 2015;3(4):444-450.
Source of Support: Nil. **Conflict of Interest:** None declared.